IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Beat Schilling et al.	) I hereby certify that this paper (and/or fee) is being electronically filed with the United States Patent and Trademark Office on this date: Dated: December 13, 2010  Zareefa B. Flener Registration No. 52,896
U.S. Serial No.	:	10/581,951	
Filed	:	08/25/2006	
Title	:	Device for Sample Preparation	
Art Unit	:	2856	
Examiner	:	Daniel Sean Larkin	

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Dear Sir:

Pursuant to the Notice of Appeal mailed July 6, 2010 and received at the USPTO on July 6, 2010, in connection with the above-identified patent application, Applicant respectfully submits the instant Brief on Appeal in accordance with 37 C.F.R. § 41.37.

I. Real Party In Interest

The above-referenced patent application has been assigned to BGB Analytic AB, who is the real party in interest to this appeal. The assignment has been recorded in the United States Patent and Trademark Office ("PTO") at Frame 0940 of Reel 018172.

II. Related Appeals and Interferences

The applicant is unaware of any related appeals or interferences.

III. Status of the Claims

Currently, claims 1-3 are pending in this application. The pending claims are presented in the **Claims Appendix** of this Brief. Claims 1-3 stand rejected. Therefore, claims 1-3 form the subject matter of this appeal.

The application on appeal was filed on August 25, 2006.

On February 12, 2008, the Office issued a first office action rejecting claims 1 and 2, among other rejections, under 35 U.S.C. §102(b) as anticipated by Villettaz et al. (U.S. 6,397,658). On April 30, 2008, the Applicant filed a response to the first Office Action amending claims 1-3, and traversing the art rejections based on Villettaz et al.

On August 11, 2008, another non-final office action issued rejecting claims 1-3 under 35 U.S.C. §102(b) as anticipated by Brewer (U.S. 6,566,145). Claim 2 was also rejected under 35 U.S.C. §103(a) as unpatentable over Pawliszyn (U.S. 2001/0032531) and claim 3 similarly rejected as unpatentable but over Pawliszyn in view of Brewer. The Applicant filed a response on November 10, 2008, further amending claim 1 and traversing the art rejections based on Brewer and Pawliszyn.

The Office issued a final office action on February 9, 2009. However, claim 1 was rejected under 35 U.S.C. §102(e) as being anticipated by Rust (U.S. 6,834,531). Claims 1 and 2 are rejected under 35 U.S.C. §103(a) as being unpatentable over Abdel-Rehim (WO 03/019149) in view of Cronin (U.S. 5,064,418). Claim 3 is rejected also as being unpatentable over Abdel-Rehim in view of Cronin and further in view of Takii et al. (JP 10-10104. Claim 3 is also rejected as being unpatentable over Abdel-Rehim in view of Reinhardt et al. (U.S. 4,849,179), and also over Abdel-Rehim in view of Cronin and further in view of Reinhardt et al. The Applicant filed a response on May 8, 2009, claims 1 and 2 were amended, claim 2 being amended only for clarity, and traversing the art rejections.

A request for continued examination was also filed, and therefore, another non-final office action issued on June 10, 2009, wherein claims 1-3 were rejected again. Claims 1 and 2 were rejected under 35 U.S.C. §103(a) as being unpatentable over Abdel-Rehim in view of Cronin. Claim 3 was rejected as being unpatentable over Abdel-Rehim in view of Cronin and further in view of Takii et al. and also further in view of Reinhardt (U.S. 4849,179). The Applicant filed a response to the office action on August 31, 2009. Claims 1-3 were amended and the art rejections were traversed.

Another office action issued on January 6, 2010, rejecting claims 1 and 2 as being unpatentable over Abdel-Rehim in view of Cronin, and claim 3 being unpatentable over Abdel-Rehim in view of Cronin and further in view of Takii et al. and also further in view of Reinhardt. This office action was made "final".

Because the Applicant and the Examiner had arrived at diametrically opposed positions, the Applicant had little choice but to file a Notice of Appeal. That notice was filed on July 6, 2010, and received by the Office on July 6, 2010. Accordingly, claims 1-3 stand rejected and form the subject of this appeal.

IV. Status of the Amendments

No amendments were filed after the final Office action. No further amendments are necessary.

V. Summary of the Claimed Subject Matter

Although reference numerals and specification citations are inserted below in accordance with 37 C.F.R. 41.37(c)(1)(v), these references numerals and citations are merely examples of where support may be found in the specification for the terms used in this section of the brief. There is no intention to in any way suggest that the terms of the claims are limited to these examples. Although, as demonstrated by the reference numerals and citations below, the claims are fully supported by the specification as required by law, it is

improper under the law to read limitations from the specification into the claims. Pointing out specification support for the claim terminology as is done here to comply with rule 41.37(c)(1)(v) does not in any way limit the scope of the claims to those examples from which they find support. Nor does this exercise provide a mechanism for circumventing the law precluding reading limitations into the claims from the specification. In short, the reference numerals and specification citations are not to be construed as claim limitations or in any way used to limit the scope of the claims.

In the invention as defined in claim 1, a method for preparation of a gaseous sample while being drawn through a hollow needle 10 into a syringe 1 for extraction and enrichment of a volatile component from the sample 16 for subsequent introduction into an analytical device is claimed, whereby for extraction of an analyte of interest the sample 16 is flushed through a stationary phase 12 located between the hollow needle 10 and the syringe 1 and having an increased volume compared to the interior of the needle 10.

In the invention as defined in claim 2, a device to carry out the method as claimed in claim 1 is claimed, wherein the device comprises a syringe 1 and a hollow needle 10 connected to a syringe body 2, wherein between the needle 10 and the syringe body 2, a chamber 9 is provided which is wider than the cross section of the needle 10 and in which a packing of an extraction material 12 for extracting an analyte of interest from a gaseous sample 16 is located.

In the invention as defined in claim 3, the device of claim 2 is further defined and specified as having: the chamber 9 is provided with a means for heating the extraction material (for instance as defined on page 3 line 36 to page 4 line 2 as being "a heating jacket 13").

VI. Grounds of Rejection To Be Reviewed on Appeal

The grounds of rejection to be reviewed on appeal are as follows:

Ground 1: The Examiner's Contention That Claims 1-2 Are Unpatentable Under 35 U.S.C. § 103(a) Over Abdel-Rehim in view of Cronin.

Ground 2: The Examiner's Contention That Claim 3 Is Unpatentable Under 35 U.S.C. § 103(a) Over Abdel-Rehim In View Of Cronin And Further In View Of Takii et al.

Ground 3: The Examiner's Contention That Claim 3 Is Unpatentable Under 35 U.S.C. § 103(a) Over Abdel-Rehim In View Of Cronin And Further In View Of Reinhardt et al.

VII. Argument

Ground 1: The Examiner Has Not Established A Case of Obviousness under 35 U.S.C. § 103(a) Against Claims 1-2.

Claims 1-2 and claim 3 are rejected under 35 U.S.C. §103(a) as being obvious and unpatentable over Abdel-Rehim in view of Cronin. The Examiner is of the opinion that modifying the syringe of Abdel-Rehim with the arrangement of Cronin would have been obvious to one of ordinary skill in the art. The Applicant submits that this is clearly in error and that the proposed modification would not have been obvious.

Abdel-Rehim discloses a method and an apparatus for sample preparation using solid phase microextraction (SPME). As explained in the Abdel-Rehim specification, Abdel-Rehim has developed a SPME system which is advantageous over previous SPME approaches. In such previous approaches, the solid phase has been placed inside the hollow needle through which a sample is taken in or ejected. Examples for this technique include a system in which the solid phase is coated on fibers which are mounted within the extraction needle according to which the interior surface of the hollow needle is coated with the solid phase extraction material. SPME devices in which the solid phase is contained inside the needle may be called "needle trap devices" as e.g. suggested in a representative article by Pawliszyn et al. In Analytical Chemistry, Vol. 73, No. 1, January 1, 2001.

Abdel-Rehim has found these traditional "needle trap" approaches to involve several disadvantages. These are explained in Abdel-Rehim on page 1, line 31 to page 2, line 3 and

on page 2, lines 11-14. Therefore, when using coated fibers, the fibers have been found to become unstable in complex matrixes; the coating on the fibers can dissolve in organic solvents; the thermal stability seems to be a problem; the recovery and consequently the sensibility is very low; and finally the absorption times are very long. For the alternative coating on the internal needle surface, the disadvantages are problems with thermal stability and the risk of a memory effect.

To avoid these disadvantages, Abdel-Rehim has suggested the so-called packed syringe solution, i.e. providing the solid phase material inside the syringe barrel.

Therefore, Abdul-Rehim clearly teaches that the packing syringe solution is supposed to constitute a major improvement over the traditional needle trap solution.

The Examiner is of the opinion that modifying the syringe of Abdel-Rehim with the arrangement of Cronin would have been obvious to one of ordinary skill in the art. This modification suggested by the Examioner, however, would involve the return to the needle trap solution which contradicts the teaching of Abdel-Rehim. No person of skill in the art would intentionally consider taking this step backwards against the direction of development and sacrifice the achievement of the improved solution taught by Abdel-Rehim.

The considerations which according to the Examiner would lead to this step backward are contrary to any logical reason. The argument "allowing the operator to utilize a good amount of stationary material without hampering the movement of the syringe piston and thus allowing for more samples to be collected" as seen on page 3, lines 2-7 of the final office action dated January 6, 2010, is absurd. Abdel-Rehim nowhere suggests that the syringe piston might be hampered by the stationary phase. Further, if the amount of sample would have to be increased, the logical way for a person of skill in the art to tackle this dilemma would be to take a larger syringe rather than putting the solid phase back into the needle.

Moreover, the amount of sample to be taken is in most cases not limited by the volume of the syringe but rather by the availability of sample.

An additional reason why a person of skill in the art would not combine Cronin with Abdel-Rehim is the fact that Cronin is not related with solid phase extraction. Cronin discloses a syringe filter, i.e. a device to be inserted between a syringe and a needle. The filter consists of hollow fibers which do not contain any absorbent. If, as suggested by the Examiner, one would place the absorbed material onto the fibers contained in the filter of Cronin, one would again arrive at the prior art with all the disadvantages which Abdel-Rehim has achieved to avoid.

The present invention is related with the same technical field as Abdel-Rehim. Like Abdel-Rehim, the inventors Schilling et al. have found certain deficiencies in the state of the art needle trap systems. But the deficiencies identified by Schilling et al. are different from those addressed by Abdel-Rehim. The inventors have found that the surface of the solid phase material in known needle trap devices is too small for optimum efficiency (English Translation of the present application, page 2, lines 4-10).

To put the solid phase into the syringe would not have been an appropriate solution, therefore, because it has some other deficiencies. Thus, if for thermal desorption it would be intended to heat the solid state material, this would not be possible because in the syringe of Abdel-Rehim, the solid phase is not separate from the solvent. Abdel-Rehim is limited to the desorption by the liquid in the syringe, which ultimately means that Abdel-Rehim is limited to liquid samples.

This is opposite the Examiner's position on page 6, first paragraph of final Office Action dated January 6, 2010. In fact, SPME cannot in all cases be used with both liquid and gaseous samples. Thus, Abdel-Rehim cannot be used for sypplying a sample to the gas chromatograph. The amount of solvent which is needed for the desorption could not be

applied to a gas chromatograph which can only take about 1-2 µl per injection. Moreover, the injection of a large amount of solvent would cover all interesting signals.

Therefore, as already provided in the After Final response dated April 19, 2010, the Applicant asserts that Abdel-Rehim is not the closest prior art. As the claimed invention is related with so-called needle trap devices for SPME such as those disclosed in the prior art mentioned in the introduction of the present application or in U.S. 2001/00325210s cited in the international search report. These devices allow the collection of solutes from a gaseous phase. In view of its limitation to liquid samples, the Applicant strenuously emphasizes that Abdel-Rehim is far more remote than these references.

At least for the reasons provided above, the Applicant submits that claim 1, a method for the preparation of a gaseous sample, and the device for performing the method as in claim 2 are non-obvious. Withdrawal of this rejection is respectfully solicited.

Ground 2. The Examiner's Contention That Claim 3 Is Unpatentable Under 35 U.S.C. § 103(a) Over Abdel-Rehim In View Of Cronin And Further In View Of Takii et al.

Claim 3 is also rejected as unpatentable over Abdel-Rehim in view of Cronin and further in view of Takii et al. The Applicant again submits that claim 3 is non-obvious and allowable. At least because claim 3 is dependent on claim 2, which is non-obvious and allowable, and in addition, the additional feature of claim 3 further distinguish it from the combination of references. Withdrawal of this rejection is respectfully solicited.

Ground 3. The Examiner's Contention That Claim 3 Is Unpatentable Under 35 U.S.C. § 103(a) Over Abdel-Rehim In View Of Cronin And Further In View Of Reinhardt et al.

Claim 3 is also rejected as unpatentable over Abdel-Rehim in view of Cronin and further in view of Reinhardt et al.. The Applicant again submits that claim 3 is non-obvious and allowable. At least because claim 3 is dependent on claim 2, which is non-obvious and allowable, and in addition, the additional feature of claim 3 further distinguish it from the combination of references. Withdrawal of this rejection is respectfully solicited.

Respectfully submitted,

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Dated: December 10, 2010

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VIII. Claims Appendix

1. A method for preparation of a gaseous sample while being drawn through a hollow needle into a syringe for extraction and enrichment of a volatile component from the sample for subsequent introduction into an analytical device, whereby for extraction of an analyte of interest the sample is flushed through a stationary phase located between the hollow needle and the syringe and having an increased volume compared to the interior of the needle.

2. A device for carrying out the method as claimed in claim 1, comprising a syringe, and a hollow needle connected to a syringe body, wherein, between the needle and the syringe body, a chamber is provided which is wider than the cross section of the needle and in which a packing of an extraction material for extracting an analyte of interest from a gaseous sample is located.

3. The device as claimed in claim 2, wherein the chamber is provided with a means for heating the extraction material.

IX. Evidence Appendix

No evidence under 37 C.F.R. § 1.130, 1.131, or 1.132 is being relied upon. The evidence relied upon is reflected in the following table.

Reference	Entered in Record
Cronin, James, US Patent 5,064,418	See PTO-892 mail by the PTO on 6/10/09, first considered by Examiner in the first Office action
Takii et al., Japanese Patent JP 10-10104 A	See PTO-892 mail by the PTO on 02/09/09, first considered by Examiner in the first Office action
Abdel-Rehim, WO 03/019149A1	See PTO-892 mail by the PTO on 02/09/09, first considered by Examiner in the first Office action
Koziel J.A., Odziemkowski M., Pawlinszyn J., *Sampling and analysis of airborne particulate matter and aerosols using in-needle trap and SPME fiber devices*, Anal Chem. Jan. 1, 73 (1): 47-54 (2001)	
Reinhardt et al., U.S. Patent 4,849,179	See PTO-892 mail by the PTO on 08/11/08, first considered by Examiner in the first Office action

Copies of the above-noted evidence are attached hereto.

X. Related Proceedings Appendix

None.

Display Settings: Abstract

Anal Chem. 2001 Jan 1;73(1):47-54.

Sampling and analysis of airborne particulate matter and aerosols using in-needle trap and SPME fiber devices.

Koziel JA, Odziemkowski M, Pawliszyn J.

Department of Chemistry, University of Waterloo, ON, Canada.

Abstract

A needle trap device (NTD) and commercial poly(dimethylsiloxane) (PDMS) 7-microm film thickness solid-phase microextraction (SPME) fibers were used for the sampling and analysis of aerosols and airborne particulate matter (PM) from an inhaler-administered drug, spray insect repellant, and tailpipe diesel exhaust. The NTD consisted of a 0.53-mm o.d. stainless steel needle having 5 mm of quartz wool packing section near the needle tip. Samples were collected by drawing air across the NTD with a Luertip syringe or via direct exposure of the SPME fiber. The mass loading of PM was varied by adjusting the volume of air pulled through the NTD or by varying the sampling time for the SPME fiber. The air volumes ranged from 0.1 to 50 mL, and sampling times varied from 10 s to 16 min. Particulates were either trapped on the needle packing or sorbed onto the SPME fiber. The devices were introduced to a chromatograph/mass spectrometer (GC/MS) injector for 5 min desorption. In the case of the NTD, 10 microL of clean air was delivered by a gas-tight syringe to aid the introduction of desorbed analytes. The compounds sorbed onto particles extracted by the SPME fiber or trapped in the needle device were desorbed in the injector and no carry-over was observed. Both devices performed well in extracting airborne polycyclic aromatic hydrocarbons (PAHs) in diesel exhaust, triamcinolone acetonide in a dose of asthma drug and DEET in a dose of insect repellant spray. Results suggest that the NTDs and PDMS 7-microm fibers can be used for airborne particulate sampling and analysis, providing a simple, fast, reusable, and cost-effective screening tool. The advantage of the SPME fiber is the open-bed geometry allowing spectroscopic investigations of particulates; for example, with Raman microspectroscopy.

PMID: 11195511 [PubMed]

United States Patent [19]

Reinhardt et al.

[11] **Patent Number: 4,849,179**

[45] **Date of Patent: Jul. 18, 1989**

[54] **APPARATUS FOR TAKING SAMPLES BY THERMAL DESORPTION**

[75] Inventors: **Karl H. Reinhardt**, Gülzow; **Helmut Dittmer**, Bleckede; **Jürgen Gandress**, Hamburg, all of Fed. Rep. of Germany

[73] Assignee: **Kernforschungszentrum Karlsruhe GmbH**, Karlsruhe, Fed. Rep. of Germany

[21] Appl. No.: **49,431**

[22] Filed: **May 14, 1987**

[30] **Foreign Application Priority Data**

May 14, 1986 [DE] Fed. Rep. of Germany 3616208

[51] **Int. Cl.**[4] **G01N 30/06**

[52] **U.S. Cl.** **422/89**; 55/67; 55/197; 55/386; 73/864.81; 73/864.91

[58] **Field of Search** 422/49, 88, 89; 436/161; 73/864.81, 864.91; 55/67, 197, 386

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,357,638	9/1944	Dwyer	422/88
3,933,431	1/1976	Trujillo et al.	422/88 X
4,003,257	1/1977	Fletcher et al.	422/89 X
4,388,272	6/1983	Gesteland	422/88 X
4,389,372	6/1983	Lalin	422/88
4,636,227	1/1987	Yin et al.	422/88 X

Primary Examiner—Barry S. Richman
Assistant Examiner—Timothy M. McMahon
Attorney, Agent, or Firm—Spencer & Frank

[57] **ABSTRACT**

An apparatus for taking samples by thermal desorption of compounds that are adsorbed on solid adsorbents contained in a sample tube. An injector has a recess for accommodating the sample tube and a connection for a capillary column of a gas chromatograph. The compounds are desorbed into such capillary column by means of a stream of carrier gas passing through the sample tube. An injector extension is fastened to the injector and has a recess for accommodating the sample tube. The recess of the injector extension is flush with the recess of the injector. A push rod is guidable in the injector extension for pushing the sample tube from a position in the injector extension into a position within the injector. A carrier gas inlet communicates with the recess in the injector extension for admitting a carrier gas therein. A plug is disposed at an end of the push rod for gripping the sample tube. The plug includes a bore for effecting communication between the carrier gas inlet and the interior of the sample tube.

8 Claims, 2 Drawing Sheets

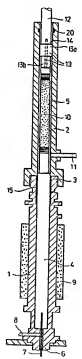

Fig. 1

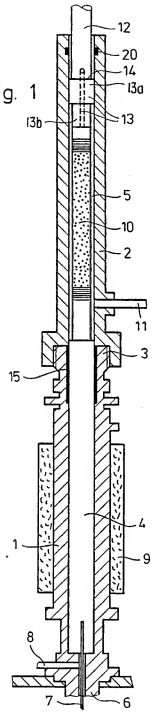
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Fig. 2

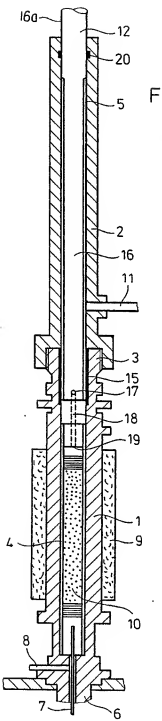
16a
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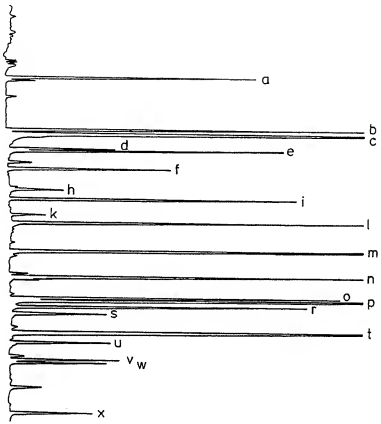
Fig. 3



APPARATUS FOR TAKING SAMPLES BY THERMAL DESORPTION

BACKGROUND OF THE INVENTION

The present invention relates to an apparatus for taking samples by thermodesorption of components that are bound to solid absorbents, wherein

(a) the absorbents are contained in a sample tube; and

(b) the compounds are desorbed into a capillary column of a gas chromatograph by means of a stream of carrier gas and by way of an injector accommodating the sample tube.

The present invention relates particularly to an apparatus for injecting into the capillary column of a gas chromatograph trace substances which have been collected in sample tubes by adsorption from air or water.

Air and water are analyzed for their content of organic trace substances by pumping a stream of the medium to be examined over an adsorber pack on which the trace substances are collected and from which they are separated again by heating or elution with a solvent. The quantity of the trace substance, that is available for analysis however, is limited by the pump hold by the electrical power available for pumping. It is therefore desirable to inject the largest possible percentage of the collected trace substances into the capillary column of the gas chromatograph. Extracts cannot be evaporated to less than 100 µl if errors due to loss of the trace substance are to be avoided. However, injecting such small solvent quantities is very difficult. If liquid samples are injected into the capillary column of a gas chromatograph, one must therefore accept that only a small portion of the extracts, at most 10 µl, can be transferred to a capillary column, thus requiring large sample quantities.

The thermosdesorption technique has been developed to transfer the trace substances collected with the aid of a solid adsorbent into the capillary columm of a gas chromatograph. All varieties of this technique have in common that the charged absorber tubes are inserted into a heated injection chamber through which flows a carrier gas and which is sealed off from the atmosphere so that the adsorbed substances can be transferred to a capillary without losses.

One prior art device is composed of a quartz sample tube having an enclosed cooling trap. The sample tube is filled with 200 mg TENAX resin from which the substances are desorbed by heating, whereupon they are frozen out in a subsequent quartz capillary by cooling with nitrogen. TENAX is a brand of porous material based on a polymer of 2,6-diphenyl-p-phenylene oxide. The desorbed components are thus concentrated into a narrow band. This desorption unit can also be used as a sample injection device for larger volumes of liquid samples which are collected with the aid of a small precolumn.

If wall influences do not matter, the precolumn may also be made of metal. Such a column, for example, has a length of 16 cm and is made of ¼" high-grade steel filled with TENAX GC 60/80 mesh. It is connected in an electric circuit as a resistor to effect resistive heating or is heated by means of a portable furnace.

If the substances are quickly released by heating, freezing may be omitted. For example, a commercially available device, operating with microwave heating, causes trace substances that are adsorbed by activated carbon, for example various ethers or Diesel fuel, to be desorbed. However, this method is limited to adsorption agents which can be heated by microwaves. Many polymers are not heated enough by such a device. For example, the adsorption agent TENAX, which is particularly suitable for collecting less volatile compounds, cannot be heated sufficiently with this device.

Many prior art injection devices contain heated valves, desorption furnaces or heated conduits. With the simpler devices, in which the adsorption sample tube is inserted into the injector, sample losses must be expected due to incomplete desorption of less volatile compounds.

Although, due to its thermal stability. TENAX is also suitable for desorption at higher temperatures, the task of transferring compounds having a higher boiling point to the capillary column by heating is accomplished only incompletely by the prior art devices.

Tests made with a commercially available thermodesorption device show that less volatile substances such as hexachlorobenzene and polychlorinated biphenyls can be transferred to the capillary column of the gas chromatograph only with considerable losses even if the carrier gas split connection is closed.

SUMMARY OF THE INVENTION

It is an ojbect of the present invention to improve the above-mentioned device so that charged adsorber tubes can be inserted into an injector in a particularly simple manner and the complete transfer of the sample substances becomes possible while avoiding stress on the adsorber and on the capillary column due to atmospheric air.

The above and other objects are accomplished according to the invention in the context of an apparatus for taking samples by thermodesorption of compounds that are bound to solid adsorbents, wherein the apparatus includes a sample tube containing solid adsorbents, and an injector having a recess for accommodating the sample tube and having a connection for a capillary column of a gas chromatography, the compounds being desorbed into such capillary column by means of a stream of carrier gas passing through the sample tube. According to the invention the apparatus additionally includes:

an injector extension fastened to the injector and having a recess for accommodating the sample tube, the recess of the injector extension being flush with the recess of the injector;

a push rod guidable in the injector extension for pushing the sample tube from a position in the injector extension into a position within the injector;

carrier gas inlet means communicating with the recess in the injector extension for admitting a carrier gas therein; and

a plug disposed at an end of the push rod adjacent to the sample tube for gripping the sample tube, the plug including a bore for effecting communication between the carrier gas inlet means and the interior of the sample tube.

With the aid of simple injector extension fastened to the injector by a threaded coupling, it is thus accomplished that the sample tube, while being heated in the injector, is not only in contact with the carrier gas but the carrier gas also flows through it will a constant flow so that all substances are directly desorbed to the capillary. The threaded coupling is suitable in principle for all injectors with splitless injection mode. The injector

extension may be fastened to the injectors of various manufacturers by means of suitable adapters. It is of particular advantage for the charged sample tube to be inserted, without the actuation of valves, into the injector through which the carrier gas flows and to be heated within the stream of carrier gas so that the adsorbed substances are directly desorbed into the capillary column. This eliminates errors due to impurities in the laboratory air. With this type of sample injection it is also possible to inject larger quantities of liquid samples. Thus, there is no longer any need to condense the extracts.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be described in greater detail below with reference to an embodiment which is illustrated in the accompanying drawings, wherein:

FIG. 1 is a longitudinal cross section of a thermodesorption device according to the invention with a charged sample tube disposed in the injector extension;

FIG. 2 is a similar view of the device of FIG. 1, with the charged sample tube disposed in the injector; and

FIG. 3 is a chromatogram of a trace substance desorbed by a desorption device according to the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

FIGS. 1 and 2 are sectional views of an injector extension 2 coupled to an injector 1. Both parts 1 and 2 have basically an elongated cylindrical shape and can be screwed to one another at adjoining ends, with a threaded coupling 3 being provided for this purpose. Each one of parts 1 and 2 is provided with a recess 4 and 5, respectively, both having the same cross section and being flush with one another. At its lower frontal face 6, injector 1 has a connection for a capillary column 7 and a split connection 8 for the discharge of a carrier gas. A heating device 9 with which the thermodesorption from a sample tube 10 filled with solid adsorbents is effected is arranged around injector 1. In the region of threaded coupling 3, injector extension 2 is connected on its side to a carrier gas intake 11 which is in communication with recesses 4 and 5.

The charged sample tube 10 is initially introduced into injector extension 2 by means of a push rod 12. A plug 13, for example of plastic, such as TEFLON, is provided for this purpose and is composed of a first portion 13a fastened to the frontal face 14 of push rod 12 and a second, smaller diameter, portion 13b inserted with a tight fit into the upper opening of sample tube 10. In this position, which is shown in FIG. 1, recesses 4 and 5 may be in communication with one another and may be rinsed, along with the exterior of sample tube 10, with a carrier gas admitted via gas intake 11.

In the injection position shown in FIG. 2, the frontal face of charged sample tube 10 is placed snuggly onto the connection of capillary column 7. To do this, sample tube 10 is transferred into recess 4 by means of push rod 12. To improve guidance and the seal against gas conduits, which are not required in this operating mode of the injector, recess 4 may be provided with a sleeve 15 in the region of threaded coupling 3, with such sleeve being adapted in a sealing manner to the outer larger diameter portion 13a of plug 13.

Following plug 13, push rod 12 has a tapered region 16 of a length which is sufficient so that, in the injection position (FIG. 2) carrier gas can flow through intake 11 and along the outside of push rod 12 toward an opening 17 in the outer jacket or surface of push rod 12. Opening 17 provides access to a bore 18 extending through push rod 12 and plug 13 to the frontal face 19 of plug 13 so that a through connection is formed for the carrier gas from inlet 11 to the head end of charged sample tube 10.

On the other hand, the length of tapered region 16 is made short enough that a reinforced region 16a of push rod 12 in the injection position of FIG. 2 is surrounded by a seal in the form of a gasket 20. Gasket 20 is embedded in the wall of interior extension 2 and prevents the escape of carrier gas to the environment and forces it through charged sample tube 10.

The quartz or glass sample tube 10, filled with TENAX and charged with the substances to be examined, has precisely the dimensions of an injector insert normally employed for sample injection with or without splitting the carries gas stream and is inserted into the heated portion of injector 1 by means of push rod 12 the plug 13 and is heated from 5 to 20 minutes at 250° C., while the capillary column is at room temperature. Push rod 12, when the the lowered position (FIG. 2), is preferably sealed against the atmosphere by means of gasket 20. When push rod 12 is raised as shown in FIG. 1, carrier gas escapes at the top of injector extension 2.

In the injector position of FIG. 2, carrier gas enters into the annular chamber between push rod 12 and injector extension 2 and is conducted through opening 17 and bore 18 to frontal face 19 to the adsorber fill of sample tube 10. Plug 13 on which tube 10 is seated, prevents the carrier gas from flowing past tube 10 on the exterior and thus forces the elution of the less volatile components. These are collected by capillary column 7 which is kept at room temperature. For hexachlorobenzene and higher boiling point substances, experience has shown that no additional cooling is necessary, it being found, surprisingly, that the peaks of the higher boiling point substances become sharp nevertheless.

FIG. 3 is the chromatogram of a standard solution of less volatile organochlorine compounds, 2 µl of which were injected into a TENAX filled sample tube 10 so that the quantities of each individual substance wele between 20 and 70 pg. Charged sample tube 10 was heated in injector 1 for 20 minutes at 250° C. with split connection 8 closed. During this time, capillary column 7 was at room temperature. The chromatogram of FIG. 3 shows sharp peaks which area approximately comparable to those obtained with on-column injection.

It will be understood that the above description of the present invention is susceptible to various modifications, changes and adaptations, and the same are intended to be comprehended within the meaning and range of equivalents of the appended claims.

We claim:

1. An apparatus for taking samples by thermal desorption of compounds that are adsorbed on solid adsorbents, the apparatus including:

a sample tube containing solid adsorbents; and

an injector having a recess for accommodating the sample tube and having a connection for a capillary column of a gas chromatograph, compounds being desorbed into such capillary column by means of a stream of carrier gas passing through the sample tube; the improvement comprising:

an injector extension fastened to said injector and having a recess for accommodating the sample

tube, the recess of said injector extension being flush with the recess of said injector;

a push rod guidable in said injector extension for pushing said sample tube from a first position in said injector extension into a second position within said injector;

carrier gas inlet means communicating with the recess in said injector extension for admitting a carrier gas therein; and

a plug disposed at an end of said push rod adjacent to said sample tube for gripping said sample tube, said plug including a bore for effecting communication between said carrier gas inlet means and the interior of said sample tube when said push rod has moved said sample tube into said injector recess.

2. Apparatus as defined in claim 1, wherein said push rod has a tapered region having an outer surface adjacent said plug; said plug has a frontal face facing the interior of said sample tube; and said bore extends from the frontal face of said plug to said outer surface of said push rod in said tapered region.

3. Apparatus as defined in claim 1, wherein said injector extension has a free frontal face and further including means for sealing the recess in said injector extension against said push rod and the environment near said free frontal face.

4. Apparatus as defined in claim 1, including means defining a threaded coupling for joining said injector extension with said injector.

5. Apparatus as defined in claim 1, wherein said carrier gas inlet means is disposed at a side of said injector extension.

6. Apparatus as defined in claim 1, including a guide sleeve fitted in the recess of said injector at the end of said injector adjacent said injector extension for guiding said plug in a sealing manner.

7. Apparatus as defined in claim 1, wherein said sample tube has a frontal face with means defining an opening, and said plug is inserted into said opening.

8. Apparatus as defined in claim 1, including means for insing recesses and said sample tube with a carrier gas when said sample tube is in said second position.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 4,849,179

DATED : July 18, 1989

INVENTOR(S) : Karl H. Reinhardt et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the title page:

In the heading of the inventors under [75], the third inventor's last name should read -- Gandrass -- .

Signed and Sealed this

Eighth Day of January, 1991

Attest:

Attesting Officer

HARRY F. MANBECK, JR.

Commissioner of Patents and Trademarks

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(74) Agent: **GLOBAL INTELLECTUAL PROPERTY**; AstraZeneca AB, S-151 85 Södertälje (SE).

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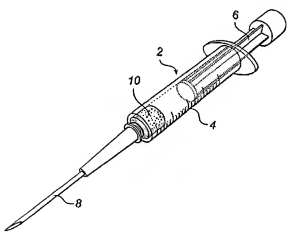
Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AI, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,*

[Continued on next page]

(54) Title: METHOD AND APPARATUS FOR SAMPLE PREPARATION USING SOLID PHASE MICROEXTRACTION



(57) Abstract: The present invention relates to a method and apparatus for use in performing sample preparation of a liquid sample using solid phase microextraction comprising the steps of drawing a liquid sample comprising analytes into a syringe having a syringe barrel provided with a solid phase material, passing the liquid sample through the solid phase material such that the analytes are adsorbed to the solid phase material; and eluting the analytes with a liquid solvent directly into the injector of an anlysing instrument. The apparatus for performing sample preparation of a liquid sample using solid phase microextraction comprises a syringe having a syringe barrel with a plunger slidable within the barrel and a hollow needle extending from the barrel. The liquid sample is drawn through the needle into the barrel wherein a solid phase material is provided in the syringe barrel to be contacted by the liquid sample drawn into the syringe.

WO 03/019149 A1

MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

METHOD AND APPARATUS FOR SAMPLE PREPARATION USING SOLID PHASE MICROEXTRACTION.

Field of the invention

The present invention relates to a method for performing on-line sample preparation using solid phase microextraction (SPME) onto a solid phase material within a syringe. The invention also relates to an apparatus for performing the sample preparation using solid phase microextraction.

Background of the invention

There is a growing realisation that faster and more efficient methods for sample pre-treatment are essential. One study showed that more than 60% of analysis time was spent in sample preparation, compared to only about 7% for actual measurement of the sample constituents. Solid phase extraction (SPE) and solid phase microextraction (SPME) are particularly attractive techniques for isolation and pre-concentration of target analytes in which very little chemical waste is produced. SPE and SPME are rapidly replacing older liquid-liquid extraction (LLE) procedures of chemical analysis.

The most significant difference between SPE and SPME lies in the fact that whereas SPE is an exhaustive extraction, i.e. the goal is to extract as near as possible to 100% of the analytes from a sample, SPME is an equilibrium extraction. Once sufficient extraction time has elapsed for the equilibrium to be established, further increases in extraction time do not affect the amount of analyte extracted. When extraction time does not impact on the results, the extraction technique is simplified and precision is improved.

In the review article "Evolution of solid-phase microextraction technology" by H. Lord and J. Pawliszyn several implementations of SPME are illustrated. The traditional approach to SPME involves coated fibers, for example, a fiber that is mounted within a hollow needle of a syringe. The fiber, for example a fused silica fiber coated with an adsorbent or a stationary phase, acts as a "sponge" to extract a sample to concentrate the organic analytes on its surface so that it can be transferred onto the heated injector of a gas chromatograph for analysis. However, there are several disadvantages of SPME using coated fibers such as that the fibers become unstable in complex matrixes such as plasma or urine. Further, samples in organic solvents can not be used as the coating on the fibers can dissolve in organic solvents. Also, the SPME coating must have a high thermal stability otherwise it cannot be used as a stationary phase. Another disadvantage with the fiber solid phase microextraction is that the recovery is very low, only somewhere between 0.5-10%, and

therefore sensitivity is low. Further, long absorption times, up to 60 minutes or more and long desorption times, up to 5 minutes are needed for extracted solutes and that will prolong the total sample analysis time.

In US 6,164,144 another implementation of the SPME technique is disclosed wherein the inner surface of a syringe needle is coated with a stationary phase for carrying out SPME. The method comprises initially contacting the coated inner surface of the hollow needle with a sample containing the analytes for a sufficient time to allow their microextraction and then placing the needle into an injection port of a chromatographic instrument and flowing a carrier gas through the fluid communication means to assist in the desorption of the analytes from the coated surface into the injection port. A disadvantage of the technique described in US 6,164,144 is that the coating must have a high thermal stability otherwise it cannot be used as a stationary phase. Also, there is a risk to get a memory effect in the stationary phase that will make it difficult to perform quantitative analysis. Further, this technique cannot be applied to a liquid chromatograph (LC) as a heated gas is used to flush the adsorbed analytes, which limits the use of analysis instruments to gas chromatographs (GC).

In cases where the analytes are present in a complex matrix, e.g. plasma, urine or samples of environmental origin, the sample preparation is of crucial importance for the analysis. The purpose of the sample preparation is to remove any interfering substances and also to enrich the analytes. The procedure must be highly reproducible with a high recovery of the target analytes. Further, an ideal sample preparation method should involve a minimum number of working steps and it should therefore be fully automated.

Summary of the invention

It is an aim of the present invention to provide an improved method and apparatus for sample preparation using solid phase microextraction where the solid phase material is provided inside a syringe barrel - a so called packed syringe. With this configuration the problem of the unstableness in the solid phase material of the coated fiber and that the coated fiber is easily damaged are avoided.

It is a further aim of the present invention to provide a method and apparatus for sample preparation in which the extraction recovery is higher than with previous methods and apparatuses. In this way, even small sample volumes can be treated.

A still further aim of the present invention is to provide a method and apparatus that can be used for analysing a sample using gas chromatography (GC), liquid chromatography (LC) or capillary electro chromatography (CEC).

A still further aim of the present invention is to provide a fully automated method and apparatus for sample preparation that consumes a very short time, i.e. 1 to 2 minutes for the treatment of each sample.

According to a first aspect of the invention there is provided a method for performing sample preparation of a liquid sample using solid phase microextraction comprising the steps of:

- drawing a liquid sample comprising analytes into a syringe having a syringe barrel provided with a solid support phase,
- passing the liquid sample through the solid support phase such that the analytes are adsorbed to the solid support phase; and
- eluting the analytes with a solvent directly into the injector of an anlysing instrument.

Preferably, the sample is drawn into the syringe using an autosampler.

Normally the adsorbed analytes are eluted directly into the analysing equipment, but if necessary, the solid support phase may be washed prior to the eluting step. Normally a washing step will be needed if the sample is drawn from a complex matrix such as plasma. The washing step is carried out using water as washing liquid.

Preferably, the analytes are eluted with an organic solvent such as methanol.

The present invention also provides an apparatus for performing sample preparation of a liquid sample using solid phase microextraction comprising a syringe having a syringe barrel with a plunger slidable within the barrel and a hollow needle extending from the barrel through which needle the liquid sample is drawn into the barrel wherein a solid phase material is provided in the syringe barrel to be contacted by the liquid sample drawn into the syringe.

Preferably, the solid phase material is provided as a porous plug inside the syringe barrel.

In another embodiment the solid phase material is provided as a coating on the inside of the syringe barrel wall.

In a further embodiment, the solid phase material is represented as a coating on a filter that is provided inside the syringe barrel.

In still a further embodiment a thin membrane made of solid phase material is provided inside the syringe barrel.

Preferably, the solid phase material is made of a solid polymer.

Preferably, the solid phase material is made of a liquid polymer.

The invention will allow for fast sample preparation with a high recovery of the target analytes. Further, this method and apparatus for sample preparation involve a minimum number of working steps and it is fully automated.

The main advantages of the present invention are that a fast sample preparation with high recovery is obtained and that it can be applied for both gas chromatography (GC) liquid chromatography (LC) and capillary electro chromatography (CEC).

A further advantage of the present invention is that the packed syringe, i.e. the syringe provided with the solid phase material, can be used several times, as much as up to a hundred times. This is possible as the solid phase material provided inside the syringe barrel can be easily and effectively cleaned.

Description of the drawings

The above and other features and advantages of the invention are defined in the claims and described in greater detail below with reference to the accompanying drawings, which illustrate preferred embodiments.

Figure 1 illustrates a syringe provided with a solid phase material for performing a sample preparation according to the present invention.

Figures 2a -2b illustrate further embodiments of the syringe according to Figure 1.

Figure 3 illustrates the syringe of Fig. 1 connected to an autosampler for drawing a liquid sample.

Figure 4 illustrates the syringe of Fig. 1 connected to an autosampler for eluting analytes into an analysing instrument.

Description of preferred embodiments

Figure 1 illustrates a syringe 2 provided with a solid phase material 10 used for preparation of a sample from a liquid sample containing analytes. The syringe comprises a barrel 4, a plunger 6 and a needle 8. The needle was fixed to have a larger inside diameter to make it possible to also handle semi-solid samples such as gels or colloids. In a preferred embodiment, the solid phase material is provided inside the syringe as a porous plug 10. Typically, the syringe is a 100-250 µl syringe. For a 250 µl syringe, preferably 1-2 mg of solid phase material is used to form the plug of approximately 3-mm in length and introduced into the syringe barrel. The solid phase material preferably consists of a silica-based material, a molecular imprinting polymer, polydimethylsiloxane or polystyrene-divinylbenzene.

In another embodiment shown in Figure 2a the inside wall of the syringe barrel is coated 11 with the solid phase material instead of it being provided as a porous plug. The coating 11 on the inside of the barrel extends 1-2 cm starting from the syringe needle.

In a further embodiment illustrated in Figure 2b the solid phase material is provided as a coating on a filter material. The coated filter material 13 is provided inside the syringe barrel as a thin disc. This embodiment has been proven to be useful when only small sample volumes are available. Instead of coating a filter, a thin membrane may be formed of the solid phase material to be used in tha same manner as the coated filter.

Turning now to Fig 3 and 4 illustrating the syringe 2 positioned in an autosampler 12 for carrying out the sample preparation. In Fig. 3, a sample is drawn by the autosampler from a bottle or container 18 on a sample tray 16 through the syringe needle 8 to the barrel 4 of the syringe. Between 10-250 µl may be drawn into the syringe, however, 50 µl is a preferred volume to draw into the syringe. When the liquid sample has passed through the solid phase material 10 the analytes have been adsorbed to the solid phase. Normally, it will be sufficient to let the liquid sample pass the solid phase material only once. However,

if necessary the liquid sample may be flushed through the solid phase material a couple of times until the analytes have been adsorbed to the solid phase.

Before the eluting step it might be necessary to remove proteins or other interfering substances from the sample. Particularly, if the sample is not in an aqueous solution the analytes need to be washed before the eluting step. The solid phase material is then washed once with water, approximately 50-100 µl, to remove any adsorbed interfering substances.

In Fig. 4, the arm 14 of the autosampler 12 has moved the syringe 2 close to the inlet port 22 of an analysing instrument 20 such as a gas chromatograph (GC) a liquid chromatograph (LC) or a capillary electro chromatograph (CEC). An organic solvent, preferably methanol in an amount of approximately 50 µl, is used to elute the analytes just before the syringe 2 is moved to the inlet port 22 of the analysing instrument 20. If a large number of samples should be prepared, i.e. more than 100, several syringes can be mounted on the autosampler arm 14. Thus, a casette carrying 2-5 syringes can be mounted on the arm.

Using the sample preparation technique according to the invention small sample volumes from 10 µl can be treated as well as large volumes up to 1000 µl. Also, a high extraction recovery of 99-100% can be obtained. Normally, using fiber SPME the extraction recovery is somewhere between 1-10%.

After the sample has been eluted the solid phase material provided inside the syringe barrel can be easily and effectively cleaned by drawing up an organic phase such as methanol or acetone though the solid phase material a couple of times (5-7 times).

A study has been performed comparing the sample preparation method using the Packed Syringe according to the invention to other sample preparation methods such as Liquid-Liquid Extraction (LLE), Solid Phase Extraction (SPE) and Fiber Solid Phase Microextraction. The results from that study are presented in the table below.

Method	Ropivacaine (μM)	Accuracy %	Precision (RSD%) (Inter-day)	Reference
Packed Syringe / GC/MS	0.15	105	7.0	
Packed Syringe / GC/MS	0.75	101	3.0	
LLE / GC-NPD	0.10	96	5.7	[1]
LLE / GC-MS	0.04	101	3.8	
SPE / LC-UV	1.90	101	3.0	[2]
Fiber SPME / GC-NPD	0.16	98	17.1	[3]
Fiber SPME / GC-MS	0.08	110	6.3	

[1] M. Engman, P. Neidenström, C. Norsten-Höög, S-J. Wiklund, U. Bondesson, T. Arvidsson, J. Chromatogr. B 709 (1998) 57-67.

[2] T. Arvidsson, Y. Askemark, M. Halldin, Biomed. Chromatogr. 13 (1999) 286-292.

[3] M. Abdel-Rehim, M. Andersson, E. Portelius , C. Norsten-Höög and L. G. Blomberg, J. Pharm. Biomed. Anal., Submitted.

GC - Gas Chromatography
LC - Liquid Chromatography
UV - Ultraviolet detection
MS - Mass Spectrometry
NPD - Nitrogen Phosphorus Detector

The foregoing is a disclosure of preferred embodiments for practicing the present invention. However, it is apparent that device incorporating modifications and variations will be obvious to one skilled in the art. Inasmuch as the foregoing disclosure is intended

to enable one skilled in the art to practice the instant invention, it should not be construed to be limited thereby, but should be construed to include such modifications and variations as fall within its true spirit and scope.

CLAIMS

1. A method for performing sample preparation of a liquid sample using solid phase microextraction comprising the steps of:
- drawing a liquid sample comprising analytes into a syringe (2) having a syringe barrel (4) provided with a solid phase material (10),
- passing the liquid sample through the solid phase material (10) such that the analytes in the sample are adsorbed to the solid phase material; and
- eluting the analytes with a liquid solvent directly into the injector (22) of an anlysing instrument (20).

2. Method according to claim 1 wherein the sample is drawn into the syringe (2) using an autosampler (12).

3. Method according to claim 1 wherein the solid phase material (10) is washed prior to the eluting step.

4. Method according to claim 1 wherein the analytes are eluted with an organic solvent.

5. An apparatus for performing sample preparation of a liquid sample using solid phase microextraction comprising a syringe (2) having a syringe barrel (4) with a plunger (6) slidable within the barrel and a hollow needle (8) extending from the barrel through which needle the liquid sample is drawn into the syringe barrel characterised in that a solid phase material (10, 11, 13) is provided in the syringe barrel (4) to be contacted by the liquid sample drawn into the syringe (2).

6. An apparatus according to claim 5 wherein the solid phase material is provided as a porous plug (10) inside the syringe barrel (4).

7. An apparatus according to claim 5 wherein the solid phase material is provided as a coating (11) on the inside of the syringe barrel wall.

8. An apparatus according to claim 5 wherein the solid phase material is provided as a coating on a filter (13) provided inside the syringe barrel (4).

9. An apparatus according to any of claims 5 to 8 wherein the solid phase material (10, 11, 13) is made of a solid polymer.

10. An apparatus according to any of claims 5 to 8 wherein the solid phase material (10, 11, 13) is made of a liquid polymer.

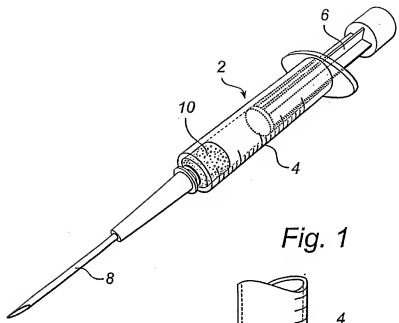

Fig. 1

Fig. 2a

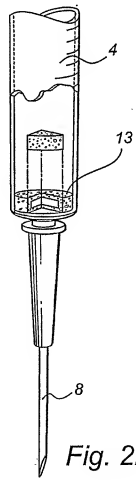

Fig. 2b

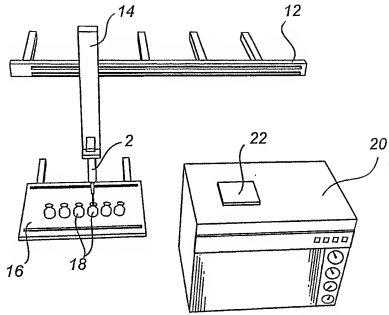

Fig. 3

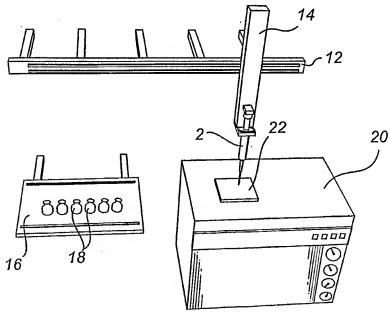

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 02/01543

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: G01N 1/40
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL,WPI,PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6164144 A (JOHN R.BERG), 26 December 2000 (26.12.00), abstract ---	1-8
A	US 5565622 A (G.E.MURPHY), 15 October 1996 (15.10.96), abstract --- ---	1-8

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 November 2002	13 -11- 2002
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Henrik Eriksson /itw Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT
Information on patent family members

30/09/02

International application No.
PCT/SE 02/01543

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6164144 A	26/12/00	EP 0961923 A	08/12/99
		IL 131185 D	00/00/00
		JP 2001513900 T	04/09/01
		WO 9931480 A	24/06/99
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㊹発明の名称　検知光学系

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明　細　書

1．発明の名称

検知光学系

2．特許請求の範囲

（1）光源と、該光源からの光をプローブ光として検知すべき物体面に導くための照射用光学手段と、該プローブ光による物体面からの反射、散乱光を検知するための検知手段と、前記物体面上のプローブ光に対応した形状の光ビームを前記光源と物体面との間の光路上に形成するためのプローブ光形成手段と、前記プローブ光と物体との相対位置を変化させるための位置変化手段と、前記プローブ光に対応した形状の光ビームの形成位置またはこれと共軛な位置に設けた前記プローブ光に対応した形状の絞りとを具備したことを特徴とする検知光学系。

（2）前記位置変化手段は、前記光路上に設けたプローブ光の照射方向を変化させるための走査光学系からなることを特徴とする特許請求の範囲第1項記載の検知光学系。

（3）前記走査光学系は回転ミラーからなることを特徴とする特許請求の範囲第2項記載の検知光学系。

（4）前記反射、散乱光は前記走査光学系を介して前記検知手段に導かれることを特徴とする特許請求の範囲第2項または第3項記載の検知光学系。

（5）前記位置変化手段は、検知すべき物体を移動させるための移動手段からなることを特徴とする特許請求の範囲第1項記載の検知光学系。

（6）前記反射、散乱光は前記照射用光学手段の光路を逆進し、該光路上に設けたビームスプリッタにより分岐されて前記検知手段に導かれることを特徴とする特許請求の範囲第1項記載の検知光学系。

（7）前記絞りは前記ビームスプリッタと物体面との間の光路上に設け、該絞りにより前記プローブ光に対応した形状の光ビームを形成するとともに前記逆進する反射、散乱光を絞ることを特徴とする特許請求の範囲第6項記載の検知光学系。

（８）前記絞りは前記ビームスプリッタと検知手段との間の分岐後の逆進光の光路上に設けたことを特徴とする特許請求の範囲第６項記載の検知光学系。

３．発明の詳細な説明

［発明の分野］

本発明はプローブ光によって物体面を走査し、その反射回折光を受光してその物体の位置情報とする光学系に関するものである。

このような光学系の一例としてはすでに良く知られている半導体露光装置のマスク（またはレチクル）とウエハとの位置合せ装置があげられる。これを縮小投影系に使用した例はｇ－ｌｉｎｅ（４３６ｎｍ）用投影光学系にＨｅ－Ｃｄレーザ（４４２ｎｍ）を使用して既に商品化され高精度な位置合せを可能としている。また、他のレーザ例えばＨｅ－Ｎｅレーザ（６３３ｎｍ）を用いた装置も知られている。

［従来技術と問題点］

従来のこの種の装置においては、プロセス上の問題により重ね合せ精度の劣化が発生している。この１つの原因としてフォトレジストの塗布の非対称性によるものがあげられる。第２図に示すようにウエハ上のアライメントマーク１の段差に対してフォトレジスト１２Ｌ，１２Ｒが塗布される。図示したようにフォトレジストの角度が左と右（１２Ｌと１２Ｒ）で非対称であると検出する信号も非対称となりアライメントマークの中心を正しく検知せずにズレた検出をしてしまう。塗布の非対称性が常に一定であれば平均的なズレとなりオフセットとして処理できるがウエハ差や、ステッパの場合のように同一ウエハの中でも多数個のショットのアライメントマークを検出する場合ショット差があれば精度劣化となってしまう。

特に、第３図に示すようにフォトレジストにより屈折されウエハで反射し、フォトレジストを出ていく光線には色々な種類のものが考えられる。例を１２Ｒの部分にとれば１回反射の光１４および２回反射の光１５……等が考えられる。光１４，１５に示されるような多重反射はフォトレジストの少しの角度変化に大きく影響される。

このような光の振舞いは、入射した光の位置が１３であるにも拘らず光が横にシフトして散乱することを意味する。したがって、精密な位置計測を行なう場合問題がある。特に光の入射位置を問題にするようなシステム、例えばプローブ光を物体に当てて、そのプローブ光の出力より物体の位置計測をするようなシステムでは検出光がプローブ光１３の位置よりずれた位置から出てきて、それがあたかも１３の位置に対応した信号であるかのように検出され、誤差を発生させる原因となっていた。

また、例えば第８図の例でエッジの散乱光を検出するシステムにおいて、プローブ光１３は未だエッジ８の位置に達していない。しかしながら、フォトレジストにより多重反射された光１５はエッジ８で散乱を受ける。このため、１３の位置にあたかも散乱エッジがあるかのように検出信号から判断される。また、フォトレジストがなくても複数個マークがある場合には第９図のようにマーク相互間で光が反射する相互作用が働く場合もある。このことも、測定精度を悪化させる原因となる。

［発明の目的］

本発明は前記従来技術の問題点に鑑みなされたものであって、プローブ光本体の位置からずれた位置の反射、散乱光は受光せず、プローブ光による位置検出の精度を高め信頼性を向上させた検知光学系の提供を目的とする。

［実施例］

本発明の一実施例を第１図に示す。

レーザ源２１から射出したレーザ光はビーム形成光学系２２により最適な径にされ偏光ビームスプリッタ２３を透過する。この実施例ではＰ偏光として効率よく透過するようにレーザ源２１を配置する。続いてλ／４板２４を透過し円偏光となった光は絞り２５を照射する。この絞り２５はプローブ光の大きさを決めるためのもので、物体面と結像関係にありこの形状により物体面でのビームの形状が決定される。絞り２５を透

過した光は振動ミラー２６により偏向されｆ－θレンズ２７により走査面に集光される。この時振動ミラー２６の反射点Ｏ₁は、ｆ－θレンズ２７の焦点位置にあるように第１図では配置されている。物体面上のプローブ光はフォトレジスト２８を通りウエハ２９上のアライメントマーク３０を走査する。

振動ミラー２６での反射点Ｏ₁にｆ－θレンズ２７の焦点位置があるため、プローブ光は物体面に垂直に入射する。物体面に当った光は平らな部分では正反射し、段差部では散乱されて、ｆ－θレンズ２７、振動ミラー２６を通して戻り絞り２５を逆向きから照射する。この時絞り２５を逆照射する光は第３図中の光線１４，１５のような多重反射光であるため横方向は拡がってもともと形成した絞り２５に相当する大きさの光より大きくなる。このような光が再度絞り２５を通ることにより多重反射により拡がった光（例えば光線１５）は遮断される。

次に入／４板２４を通りＳ偏光となって偏光ビームスプリッタ２３で反射され結像レンズ３１を通って振動ミラー２６の反射点Ｏ₂と共役な位置Ｏ₃に配置された空間周波数フィルタ３２で正反射光が遮断され散乱回折光が暗視野信号として光電変換器（ディテクタ）３３により受光される。

以上のように第１図では行きには絞り２５でビーム形状を決め、戻りには広がったビームを再度形状決めを行なう再結像用の光学系で第３図中の光線１４，１５……を受光しないことを可能としている。

このようにして本発明の目的は達成される。

第１０図に、プローブ光を直接走査光学系で走査するのではなく、プローブ光を止めておいて物体を動かして計測する例を示す。８０はレーザ源でビーム形成光学系８１により９７の位置にプローブ光のもととなる集光位置を形成する。集光位置９７でのビーム形成をディフラクションリミットな系で行なえば、９７の位置に物に絞りを設けなくても所望のビーム形状が得られる。光学系８１は通常のレンズでもシリンドリカルレンズでも良く、シリンドリカルレンズの場合には９７の位置にスリット状のビームが形成される。

集光位置９７から光は発散し始めビームスプリッタ８２、リレーレンズ８３を通って対物レンズ８５に入射し、集光位置９７と共軛な位置９８に９７に対応したプローブ光を形成する。図中、斜線で示した光束が入射ビームを示し、対物レンズの有効径より小さい光束径となっている。検知しようとする物体８６は例えばウエハであるが第２図に示したような多重反射による精度悪化要因をもっている。これは９８の位置にあるべきビームが多重反射により横ズレし、９８から離れた位置で散乱され、あたかも散乱位置が９８にあるようにみせてしまうという前述した理由による。物体８６は載置台８７の上に載っておりステージ８８の移動によりプローブ光との相対位置関係を変化させる。８９はステージ８８上に置かれた固定ミラーでレーザ干渉計９０と共に物体の座標をモニタする。プローブ光は正反射光、散乱光、多重反射光を総てとりまとめて反射し、対物レンズ８５に戻り、ミラー８４、リレーレンズ８３を通ってハーフミラー８２で反射され、フィールドレンズ９１を通過する。フィールドレンズ９１は対物レンズ８５の焦点位置ＡをＢの位置に結像させる。Ｂの位置には空間周波数フィルタ９２がおかれており、斜線で示された光束すなわち、入射光束に対する平らな面での反射成分である正反射光をカットする。空間周波数フィルタ９２を通過した光は従って散乱光（回折光）と多重反射光となる。光は結像レンズ９３により再び９４の位置に結像される。この９４の位置は９７の位置と共軛であり、従ってここに９７の大きさに対応した視野絞りを設置すれば多重反射光成分は横ずれしているため、９４の位置の絞りで遮断される。実際９４の位置で観察されるプローブ光は多重反射のためもとの９７に対応するビーム形状より大きくなっているのが通例である。９４を通過した光がエッジで散乱回折した光であり、これをレンズ９５でフォトディテクタ９６に導く。すなわち、第１０

図の光学系で物体を走査すればプローブ光がエッジにさしかかった時にのみフォトディテクタ９６で出力が観察される。このように必ずしも再結像光学系を設けなくても本発明の目的は達成される。第１図の光学系では２回目に絞りを通った時、絞りにより回折光が発生する可能性があり、場合により検知すべきマークに工夫を要するが、第１０図の光学系ではそのような制約はない。

第４図に投影光学系の場合での実施例を示す。

第１図の場合と同じように絞り１００により２回ビームを形成する。第４図は本発明を焼付装置に適用した例を示す。

図中、５０はマスク、５１はウエハで、投影レンズ５２はマスク５００の像をウエハ５１上に等倍または縮小投影する。λ／４板５２ａは偏光方向によってマスク反射とウエハ反射を分けるために設ける。

マスク５０とウエハ５１には、第５図に示すＡＡパターンを各２個ずつ設ける。例えばドット状のエレメントをウエハに、実線のエレメントをマスクに設ける。

５３はレーザ光源で、紙面内に直線偏光しているものを使用する。５４はポリゴンミラーで等速回転する。５５はｆ－θレンズでレーザビームを等速走査するのに役立つ。５８は走査範囲分割プリズムで、このプリズムはビームの一回の走査の前半と後半を２つのＡＡパターンのそれぞれに充当する。以下の系は左手系と右手系が対称であるから同じ番号を付ける。

６４は反射率の小さな半透鏡、６５は偏光ビームスプリッタ、６６はコンデンサレンズ、６７は観察用光源である。６８はリレーレンズ、６９は反射部材、７０は空間周波数フィルタ、７１は集光レンズ、７２は受光素子で、マスク５０から来る光を受光する。７３は顕微鏡対物レンズ（以下、対物レンズ）で、マスク５０とウエハ５１とのＡＡマークを見込む位置にセットされている。

以上の構成で、レーザ光源からのレーザビームはポリゴンミラー５４へ入射してここで走査される。振れ走査されたレーザビームはｆ－θレンズ５５で平行走査に変換された後、ビームスプリッタ５７を透過してダハプリズム５８へ入射し、例えば始めプリズム５８の左斜面で反射して左側へ向い、途中から右斜面で反射して右側へ向う。プリズム５８で反射したビームはプリズム５９で反射し、半透鏡６４を透過して対物レンズ７３へ入射してマスク５０上に集光され、更に投影レンズ５２を介してウエハ５１上に集光され、両者を走査する。まずマスク５０のＡＡパターンで反射された光は対物レンズ７３へ入射し、続いて半透鏡６４で反射する。

ここで反射した光は偏光板６５へ入射し、マスク５０で反射し紙面内にある直線偏光光は透過し、ウエハ５１で反射し、紙面に垂直な直線偏光光は６５で阻止される。透過光はリレーレンズ６８と反射部材６９を経た後、直接反射成分はフィルタ７０で遮断され、ＡＡパターンで散乱された成分は集光レンズ７１で集光されて受光素子７２に入射し、マスク側のＡＡ信号となる。

次にマスク５０を透過した走査ビームは投影レンズ５２を屈折透過する際にλ／４板５２ａに入射し、円偏光に変換され、ウエハ５１上を走査する。ウエハ５１のＡＡパターンで反射された光は逆方向からλ／４板５２ａを透過する際に先程とは方向が９０°回転した直線偏光となり、対物レンズ７３と半透鏡６４を経てダハプリズム５８を反射し再度ポリゴン５４により反射される。そして前述のように再度絞り１００を通過し偏光ビームスプリッタ１０３へ入射する。λ／４板５２ａによって図面に平行な直線偏光になっているからウエハ５１の反射光は偏光ビームスプリッタ１０３で反射し、集光レンズ１０４を経てフィルタ１０１の透明部で透過してディテクタ１０２へ入射する。

このようにして取り入れたＡＡ信号と受光素子７２のマスク側ＡＡ信号に基づいて演算を実行し、その結果（ｘ，ｙ，θ誤差）により補正機構８１を駆動し、マスクチャック８２を移動させてマスク５０とウエハ５１のアライメントを達成する。但し、マスク５０の替りにウエハ側を移動し

ても良い。

なお、本発明は物体面に相当する絞りおよび瞳面に相当する絞りの２重のフィルタリング系が特徴であるが、ここで述べた実施例の他にも絞りのかけ方により種々の変形が存在する。第６図に示すように、レーザ源２００から射出したビームはビームエキスパンダ２０２によって拡げられて絞り２０１を透過して偏光ビームスプリッタ２０３を透過する。前述のようにウエハを走査した反射光は偏光が９０°回転し偏光ビームスプリッタ２０３を反射し絞り２０４を透過する。この時絞り２０１と絞り２０４は別々のものでも光学的に結像関係の位置に配置すればよい。偏光ビームスプリッタを使用するのは光量を効率良く使用するためで、光量が十分であれば、ハーフミラー等を使用することも何等問題とならない。

また、第６図に示すように絞りを走査面と結像関係の位置に配置する視野絞りとする代りに、第７図のように、瞳面に配置する開口絞り２０５とし、その回折限界で走査するビームの形状を決めることも考えられる。その時も受光側の絞り２０４は配置することができるが、この時絞り２０４は前述の絞り２０５とは結像関係にはない。しかし、絞り２０４は視野絞りとして使用されるので本発明の目的は達成される。なお、２０６はビームスプリッタである。

また、第４図までの実施例は瞳視野検出について示したが瞳に関するフィルタリングの特殊例として明視野検出としても同様である。この視野絞りを走査するビーム径より小さくして分解能を上げることが可能となる。

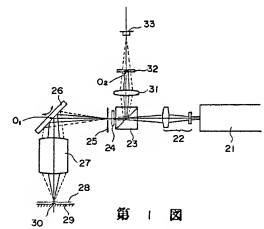
［発明の効果］

以上説明したように、本発明においては、プローブ光に対応した形状の光ビームの形成位置またはこれと共軛な位置に絞りを設け、光路を逆進する多重反射の反射、散乱光を遮断しているため、プローブ光照射位置以外からの多重反射光による検知位置精度の低下が防止され、位置検出の信頼性が高まる。

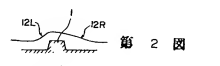
４．図面の簡単な説明

第１図は本発明実施例の構成図、第２図はフォトレジスト塗布状態の説明図、第３図は多重反射の説明図、第４図は本発明の別の実施例の構成図、第５図は検知マークの一例を示す上面図、第６図および第７図は各々本発明のさらに別の実施例の構成図、第８図はプローブ光と反射、散乱光の説明図、第９図はマーク相互間での反射光の説明図、第１０図は本発明のさらに別の実施例の構成図である。

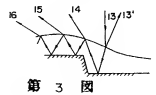
２１，５３，８０，２００……レーザ光源、
２５，９４，１００，２０１，２０４，２０５……絞り、
３０……アライメントマーク、
３３，９６，１０２……ディテクタ。



第１図

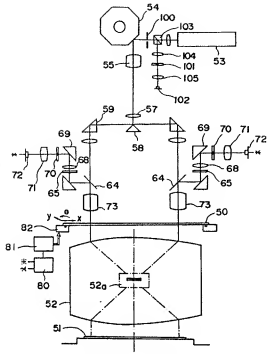


第２図

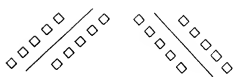


第３図

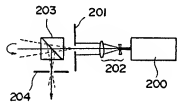
特許出願人　キヤノン株式会社
代理人　弁理士　伊東哲也
代理人　弁理士　伊東辰雄



第 4 図



第 5 図



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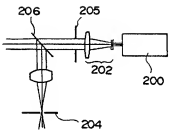

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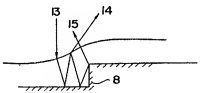
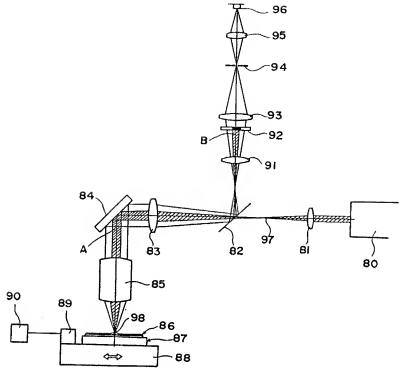


第 8 図

第 9 図



第 10 図

United States Patent [19]

Cronin

[11] Patent Number: 5,064,418

[45] Date of Patent: Nov. 12, 1991

[54] FILTER MEANS FOR USE WITH SYRINGE AND NEEDLE

[75] Inventor: James J. Cronin, Mission Viejo, Calif.

[73] Assignee: Microgon, Inc., Laguna Hills, Calif.

[21] Appl. No.: 506,546

[22] Filed: Apr. 4, 1990

Related U.S. Application Data

[63] Continuation of Ser. No. 860,104, May 6, 1986, abandoned, which is a continuation-in-part of Ser. No. 762,259, Aug. 5, 1985, abandoned.

[51] Int. Cl.[5] A61M 5/00

[52] U.S. Cl. 604/190

[58] Field of Search 604/190, 187

[56] References Cited

U.S. PATENT DOCUMENTS

4,014,797	3/1977	Raines et al.	604/190 X
4,267,053	5/1981	Hashino et al.	604/190 X
4,453,927	6/1984	Sinko	604/190 X

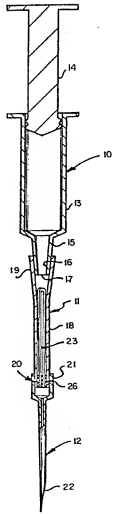
Primary Examiner—John D. Yasko

Attorney, Agent, or Firm—Paul R. Wylie

[57] ABSTRACT

According to this invention, there is provided a filter device adapted to be used with a syringe and a needle wherein longitudinally positioned hollow filter fibres and a flow blocking material are arranged within the tubular body for directing flow through the material of the hollow fibres. The device according to the invention can be embodied either as a single filter element or as a combination syringe, filter and needle.

2 Claims, 3 Drawing Sheets



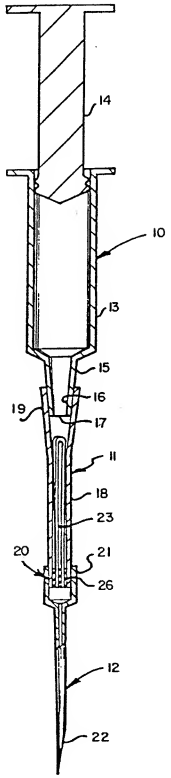


FIG.1

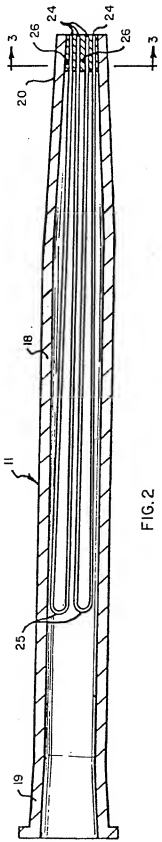


FIG. 2

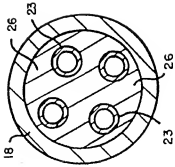


FIG. 3

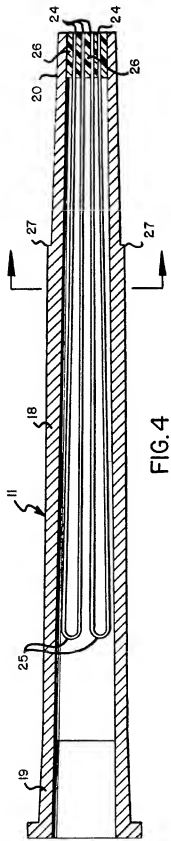


FIG. 4

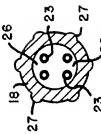


FIG. 5

FILTER MEANS FOR USE WITH SYRINGE AND NEEDLE

This is a continuation of copending application Ser. No 06/860,104, filed on May 6, 1986, now abandoned, which is a continuation-in-part of Ser. No. 06/762,259, filed on Aug. 5, 1985, now abandoned.

BACKGROUND OF THE INVENTION

This invention relates generally to a filtering device adapted to be used with a syringe and a needle; and, in another embodiment of the invention, to a combination syringe, needle and filter.

The current state of the art of syringe filters is believed to involve the use of a round flat sheet microporous membrane that is sealed between two plastic halves as an intermediate filter typically for use between a syringe and needle. If air is introduced to the syringe side of one of these filters and pressure is applied, the air is compressed over the entire surface area of the membrane thus substantially blocking or minimizing the flow of fluid. It will be appreciated, that if liquid is introduced to the syringe side of the flat filter (which is horizontal to the vertical axis of the syringe and needle), the liquid will only cover the entire surface of the membrane, in most cases, if the syringe and needle are in a vertical position. If the syringe and needle are in a horizontal position, or angled, the liquid may only cover part of the surface of the membrane thus causing air blockage. Moreover, increased filtering capacity of such filters can only be attained by increasing the diameter resulting in filters having dimensions that sometimes exceed the diameters of the syringe barrels to which they are attached and result in awkward handling.

In recent years, attempts to devise various syringe filters have resulted in that shown in U.S. Pat. No. 4,316,462 which discloses an adapter which extends between the needle that is already in place on the syringe and a second needle. A flat membrane filter is used in this adapter.

According to this invention, there is provided a filtering device adapted to be used with a syringe and a needle wherein longitudinally positioned hollow filter fibres and a flow blocking material are arranged within the tubular body for directing flow through the material of the hollow fibres. The device according to the invention can be embodied either as a single filter element or as a combination syringe, filter and needle.

The foregoing arrangement produces the advantage that, even though the syringe and needle are tipped from vertical during use, the fluid will pass through the filter fibers tangentially to the longitudinal axis of the filter, thus eliminating air blockage. If air is present, any air blockage that will occur will be minimal compared to the flat membrane filters.

SUMMARY OF THE INVENTION

According to this invention, there has been provided a filtering device adapted to be used with a syringe and needle including an elongate tubular body having a first mounting means on the end thereof adapted to be sealingly connected to the needle mounting on said syringe and a second mounting means on the opposite end thereof adapted to be sealingly connected to the cooperative syringe mounting means on said needle. Elongate microporous hollow filter fibres are arranged within said tubular body with said fibres being closed at one end thereof and open at the opposite thereof. A flow blocking material is arranged around said fibres blocking flow through said tubular body other than through the material of the hollow fibres.

In accordance with another aspect of the invention, there is provided a combination syringe, needle and filter utilizing a filter of the foregoing type between the syringe and the needle.

It was an object of this invention to provide a filter for a syringe and needle whereby the fluid drawn into the syringe through the needle or ejected from the syringe through the needle was filtered by a filter means intermediate the syringe and needle.

A further object of this invention was to provide a filter of the foregoing type which would eliminate or minimize air blockage.

A still further object of this invention was to provide a filter for use with a syringe and needle that would be easy to manufacturer and convenient to use.

These and other objects of the invention will be evident from the following more detailed description of the invention.

DESCRIPTION OF THE DRAWINGS

The invention will be more fully understood and described with reference to the drawings wherein:

FIG. **1** is a view in cross-section of a syringe, needle and filter according to the invention;

FIG. **2** is a cross-sectional view of the filter according to the invention;

FIG. **3** is a view in cross-section taken on lines **3—3** of FIG. **2**;

FIG. **4** is a view similar to FIG. **2** showing an alternate embodiment of the invention; and,

FIG. **5** is a view in cross-section taken on lines **5—5** of FIG. **4**.

DETAILED DESCRIPTION OF THE INVENTION

There is shown in FIG. **1** an arrangement according to the invention including a syringe **10**, a filter **11** and a needle **12**. The syringe has a barrel member **13** and a plunger element **14**. The syringe includes a male needle mounting means **15** having a conical surface **16** that is normally adapted to mate with a mounting means on a needle such as needle **12**. Conical surface **16** terminates in opening **17**. Filter **11** includes an elongate tubular body **18** having a first mounting means **19** of outwardly tapered concial configuration adapted to mate with conical surface **16** of syringe **10** in a fluid sealing manner. At the opposite end of elongate tubular body **18** there is a second mounting means **20** of inwardly tapered conical configuration adapted to mate with corresponding mounting means of a needle such as needle **12**.

Needle **12** includes an outwardly tapered female mounting means **21** of conical configuration and cannula **22**.

Mounted inside elongate tubular body **18** are elongate microporous hollow filter fibres **23**. As best shown in FIG. **2**, hollow fibres **23** have an open end **24** and a closed end **25**. While a single fibre can be used having an open end and a sealed closed end, the arrangement shown in FIG. **2** wherein a fibre is looped back upon itself to form two open ends **24**, with the loop providing closed ends **25**, is preferred.

Flow blocking material **26** is arranged to position hollow filtering fibres **23** in elongate tubular body **18**

such that flow through tubular body **18** other than through the material of hollow filtering fibres **23** is blocked. It is preferred to have the blocking material **26** in this position to provide a reservoir of fluid upstream of said material in said elongate tubular body **18** to promote transverse flow of said fluid material through the material of hollow filter fibres **23**.

In a preferred form of the invention, the concial surfaces of elements **16**, **19**, **20** and **21** all have a conical angle of from about 1' to about 2'.

The elongate tubular body **18** of filter **11**, in its referred form, should not exceed the diameter of a barrel member **13** of syringe **10**.

In a preferred form, the total length of filter unit **11** will be about 0.5 inches to about 4 inches with a preferred outside diameter in the range of about 0.10 inches to about 0.30 inches with an inside diameter approximating about 0.05 inches to about 0.20 inches. The ratio of length to the outside diameter of filter will be in the range of about 2 to about 20.

The microporous hollow fibres **23** can be of any length, preferably up to and including the length of tubular body **18** less the depth of protrustion of the male needle mounting means **15** which otherwise might damage the fibres. The fibres **23** can also be relatively short in length compared to the length of tubular body **18** provided that sufficient filtration surface is present for the particular application.

The porosity rating of fibres **23** is in the microporous range of about 0.05 to about **1** microns. A preferred range is about 0.1 to about 0.45 microns.

The inside diameter for fibres **23** can be from about 0.008 inches to about 0.08 inches with a preferred inside diameter being in the range of about 0.012 inches to about 0.05 inches with a further preferred diameter being about 0.18 10%. It has been found in accordance with the invention that larger fibres under the pressures applied by injection force on the syringe may collapse. Smaller diameter fibres also increase the packing density. The outside diameter should be that which will result in a wall thickness of about 0.001 inches to about 0.005 inches with a preferred wall thickness being about 0.0015 inches to about 0.004 inches.

Flow blocking potting material **26** can be selected from the group consisting of silicone, polyurethane, epoxy, and cyanoacrylate ester resins with polyurethane being the currently preferred potting material. Elongate tubular body **18** in its preferred form is made out of a rigid plastic material, preferably transparent or transluscent, such as an acrylic or polycarbonate resin.

The effective filtration area of the microporous hollow fibres **23** in a given filter element **11** is in the range of about 0.25 cm^2 to about 10 cm^2 with a preferred range being about 5.0 cm^2 or less. The effective filtration area is measured on the inside walls of the fibres.

The porosity of fibres **23** should be greater than about 50% with a preferred range being about 65% to 85% with the upper range of porosity being limited at a point where the fibres have no structural integrity.

Packing density of fibres **23** in tubular body **18** as expressed in a ratio of cross-sectional areas of fibres to cross-sectional area of the lumen of tubular body **18** should be less than about 60%. The number of fibres **23** in tubular body **18** is preferably between **1** and **10** and more preferably between 2 and 8.

In FIG. 4, there is shown an alternate embodiment according to the invention wherein the elongate tubular body is tapered, in this case, at an angle of about 1' to about 3' and wherein there are also included finger grippable projections in the form of an elongate ribs **27**. These ribs extending substantially the length of the tubular portion **18** of filter unit **11**. The existence of ribs **27** make it not only easier to grip the filter when it is connected with needle **12** and syringe **10**, but further make it easier to install on the syringe and to facilitate removal and connection with needle **12**.

An added advantage of the elongate filter **18** of the invention is that the filter itself will fit into ampoules for the withdrawal of liquids therefrom. The filter, therefore, has the advantage of filtering either in asperation or injection of fluids.

As best shown in FIG. **5**, grips **27** can be spaced equal distance around tubular body **18** and it is preferred to have such ribs projecting from said tubular body at a distance in the range of from 0.008 to 0.015 inches. The elongate ribs **27** are themselves tapered and it is preferred that the angle of taper be from about 1.0 to about 1.5 degrees. The taper of the tube **18** and the ribs **27** facilitate manufacture of the filter by the injection molding process whereby the parting line can be at the face **28** of a standard luer fitting **29**. It is also preferred, to have the interior of tube **18** tapered at an angle substantially the same as that of the exterior to provide for easy removal from mold parts in the injection molding process.

The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The present embodiments are therefore to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description; and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

I claim What is claimed is:

1. A filtering device, adapted to be used with a syringe and a needle, for filtering fluids drawn in or ejected from said syringe, said filtering device comprising:

(a) An elongate tubular body having a first mounting means on one end thereof adapted to be sealingly connected to the needle mounting on said syringe and a second mounting means on the opposite end thereof adapted to be sealingly connected to the cooperative syringe mounting means on said needle;

(b) Elongate microporous hollow filter fibres arranged longitudinally within said tubular body, said fibres being closed at one end thereof and open at the opposite end thereof; and,

(c) Flow blocking material arranged around said fibres for blocking flow through said tubular body other than through the material of said hollow fibres, said flow blocking material being provided at a position in said elongate tubular body to provide with said elongate microporous hollow filter fibres a reservoir of fluid around said hollow filter fibres to promote transverse flow of said fluid through the material of said hollow filter fibers,

(d) Said first mounting means being adapted to be connected to a male needle mounting means of conical configuration of a syringe and said second mounting means being adapted to be sealingly connected to a female mounting means of conical configuration of a needle, said first and second mounting means being conical in configuration and

adapted to mate with corresponding conical portions of said needle mounting means and said needle, the conical angle of said concial mounting being about 1' to 2', said flow blocking material being located in said tubular body adjacent the end of said tubular body having said second mounting means, the open end of said elongate microporous hollow fibres being adjacent the end of said tubular body having said second mounting means, the ratio of length to the outside diameter of said elongate tubular body being in the range of about 5 to 20, the porosity rating of said fibres being in the range of about 0.05 to about 1 micron and the packing density of said fibres being less than about 60%, the porosity of said fibres being greater than about 50%, the effective filtering area of said fibres being about 1 cm to about 10 cm the total length of said filtering device beinb about 0.5 inches to about 4 inches, the outside diameter of said elongate tubular body being about 0.10 inches to about 0.30 inches and, the inside diameter of said elongate tubular body being about 0.05 inch to about 0.20 inches.

2. A combination syringe, filter and needle comprising:

(1) a syringe having a mounting means thereon;

(2) a needle having a mounting means thereon;

(3) a filter for filtering fluids drawn in or ejected from said syringe, said filter comprising:

(a) an elongate tubular body having a first mounting means on one end thereof adapted to be sealingly connected to the needle mounting on said syringe and a second mounting means onthe opposite end thereof adapted to be sealingly connected to the cooperative syringe mounting means on said needle;

(b) elongate microporous hollow filter fibres arranged longitudinally within said tubular body, said fibres being closed at one end thereof and open at the opposite end thereof; and,

(c) flow blocking material arranged around said fibres for blocking flow through said tubular body other than through the material of said hollow fibres, said flow blocking material being provided at a position in said elongate tubular body to provide with said elongate microporous hollow filter fibres a reservoir of fluid around said hollow filter fibres to promote transverse flow of said fluid through the material of said hollow filter fibers,

(d) said first mounting means being adapted to be connected to a male needle mounting means of conical configuration of a syringe and said second mounting means being adapted to be sealingly connected to a female mounting means of conical configuration of a needle, said first and second mounting means being conical in configuration and adapted to mate with corresponding conical portions of said needle mounting means and said needle, the conical angle of said conical mounting being about 1' to 2', said flow blocking material being located in said tubular body adjacent the end of said tubular body having said second mounting means, the open end of said elongate microporous hollow fibres being adjacent the end of said tubular body having said second mounting means, the ration of length to the outside diameter of said elongate tubular body being in the range of about 5 to 20, the porosity rating of said fibres being in the range of about 0.05 to about 1 micron and the packing density of said fibres being less than about 60%, the porosity of said fibres being greater than about 50%, the effective filtering area of said fibres being about 1 cm to about 10 cm the total length of said filtering device being about 0.5 inches to about 4 inches, the outside diameter of said elongate tubular body being about 0.10 inches to about 0.30 inches and, the inside diameter of aid elognate tubular body being about 0.05 inch to about 0.20 inches.

* * * * *